
Pluripotency and the Transcriptional Inactivation of the Female Mammalian X Chromosome.

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Public Summary:

X chromosome inactivation (XCI) is a striking example of developmentally regulated, wide-range heterochromatin formation that is initiated during early embryonic development. XCI is a mechanism of dosage compensation unique to placental mammals whereby one X chromosome in every diploid cell of the female organism is transcriptionally silenced to equalize X-linked gene levels to XY males. In the embryo, XCI is random with respect to whether the maternal or paternal X chromosome is inactivated and is established in epiblast cells upon implantation of the blastocyst. Conveniently, ex vivo differentiation of mouse embryonic stem cells (mESCs) recapitulates random XCI and permits mechanistic dissection of this stepwise process that leads to stable epigenetic silencing. Here, we focus on recent studies in mouse models characterizing the molecular players of this female-specific process with an emphasis on those relevant to the pluripotent state. Further, we will summarize advances characterizing XCI states in human pluripotent cells, where surprising differences from the mouse process may have far-reaching implications for human pluripotent cell biology.

Scientific Abstract:

X chromosome inactivation (XCI) is a striking example of developmentally regulated, wide-range heterochromatin formation that is initiated during early embryonic development. XCI is a mechanism of dosage compensation unique to placental mammals whereby one X chromosome in every diploid cell of the female organism is transcriptionally silenced to equalize X-linked gene levels to XY males. In the embryo, XCI is random with respect to whether the maternal or paternal X chromosome is inactivated and is established in epiblast cells upon implantation of the blastocyst. Conveniently, ex vivo differentiation of mouse embryonic stem cells (mESCs) recapitulates random XCI and permits mechanistic dissection of this stepwise process that leads to stable epigenetic silencing. Here, we focus on recent studies in mouse models characterizing the molecular players of this female-specific process with an emphasis on those relevant to the pluripotent state. Further, we will summarize advances characterizing XCI states in human pluripotent cells, where surprising differences from the mouse process may have far-reaching implications for human pluripotent cell biology.

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